**SUPPLEMENTARY MATERIAL**

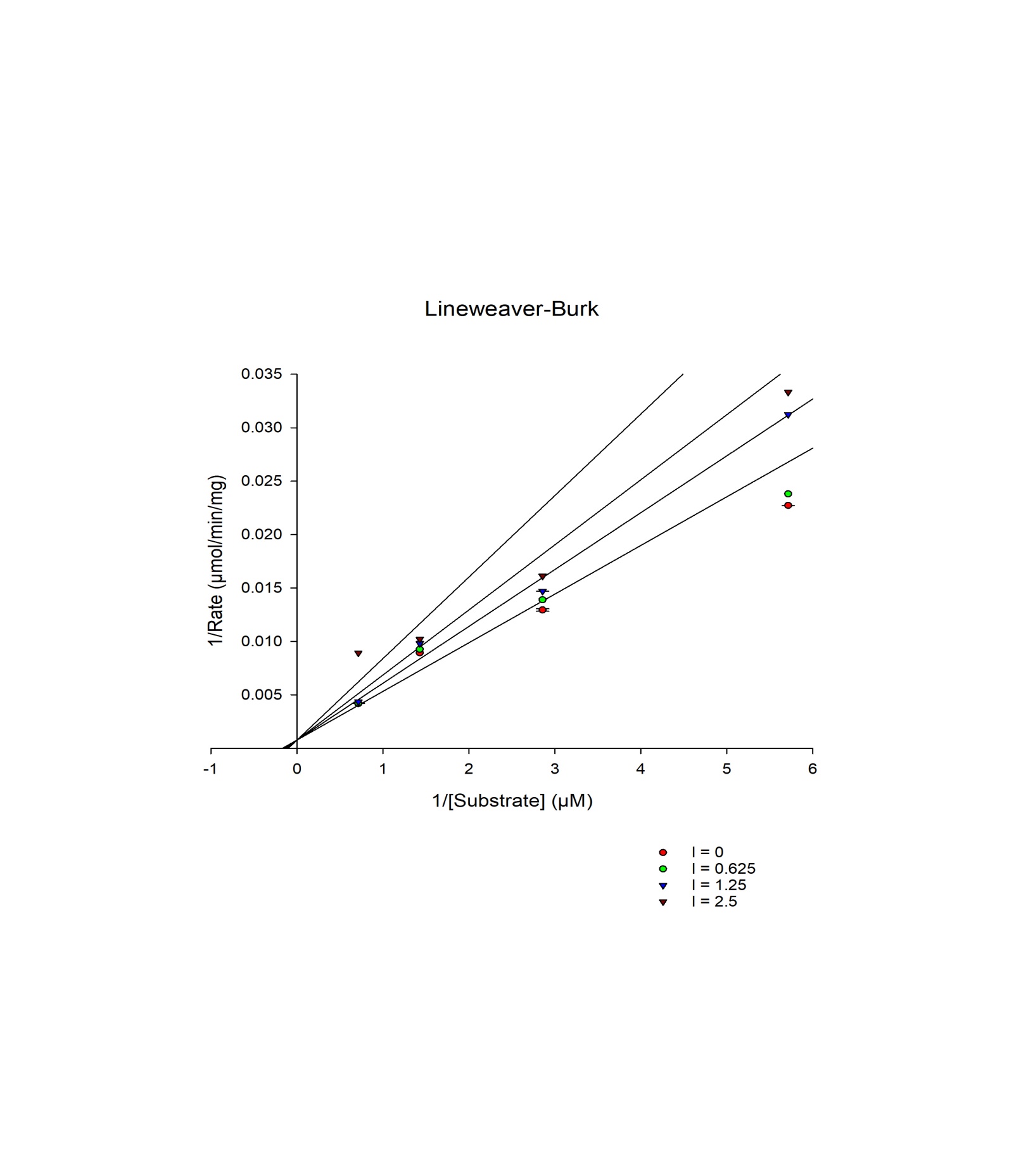
**Synthetic Benzofuran-linked Chalcones with Potential Therapeutic Approach to Manage Diabetes Mellitus**



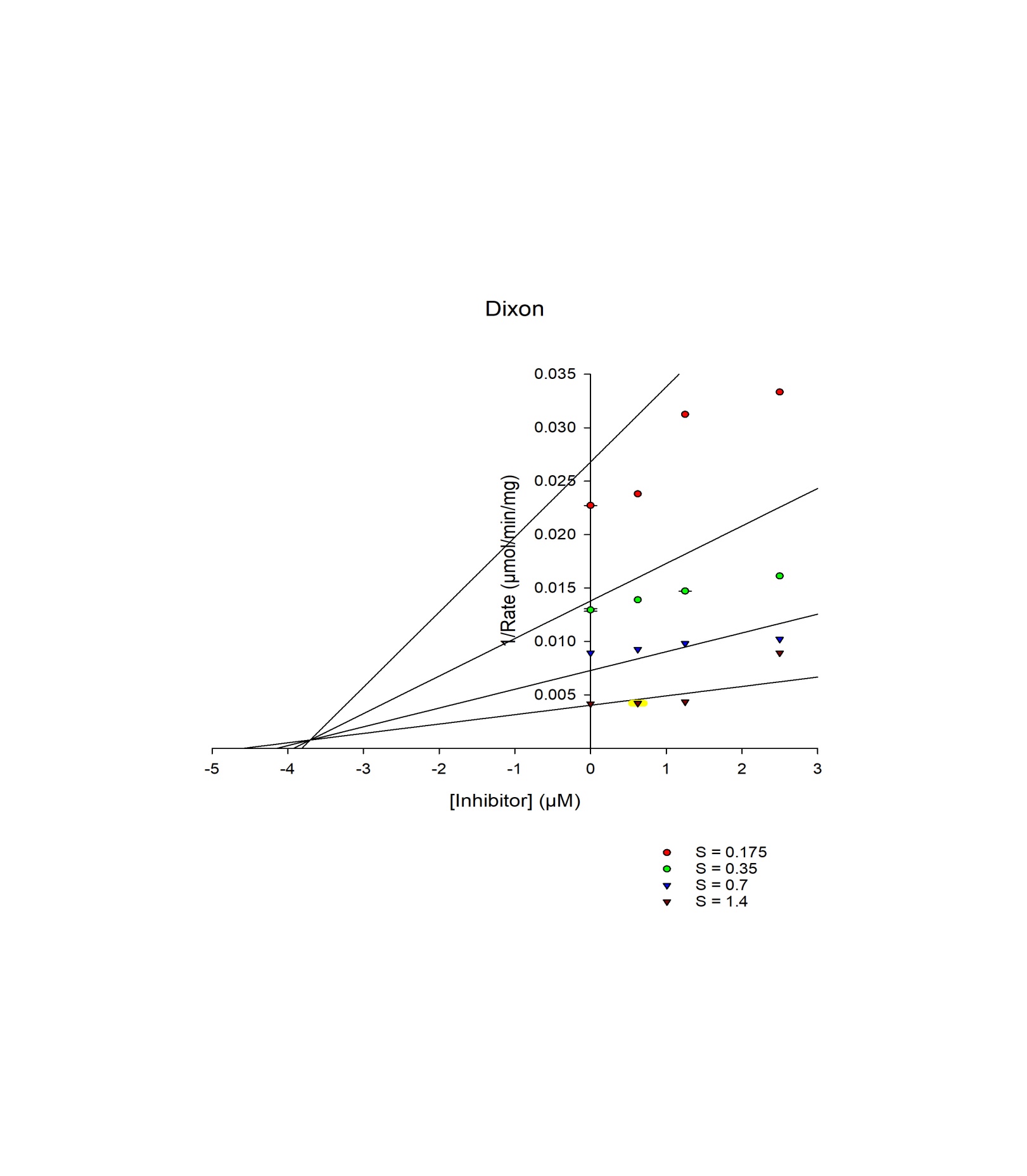
**Figure-S1:** Comparison of structures and *α*-amylase inhibitory activity of molecules **20-26**.



**Figure-S2:** Comparison of structures and *α*-amylase inhibitory activity of analogs **27-33**



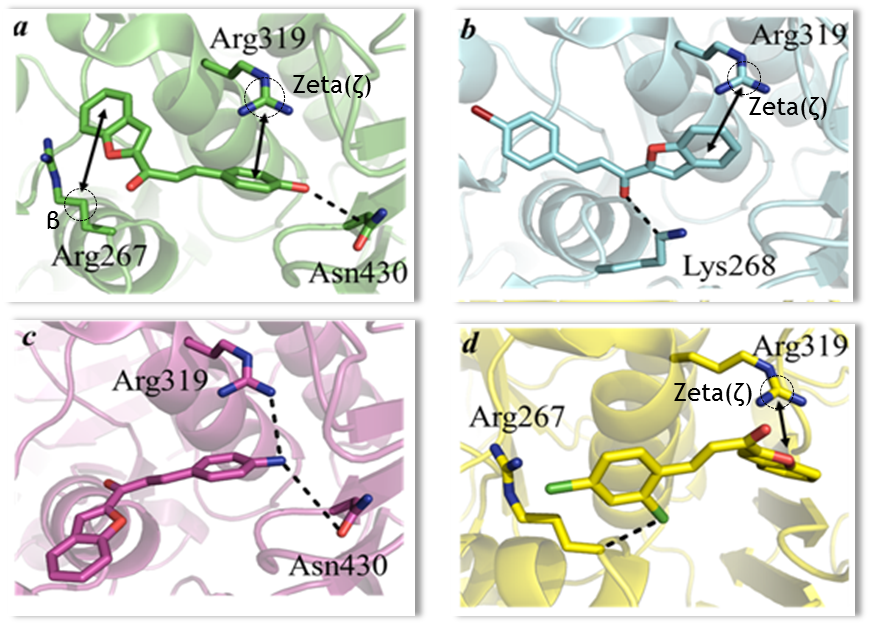
**Figure-S3:** Graph of compound **2**; Lineweaver-Burk plot of the reciprocal of rate of reaction (velocities) vs reciprocal of the substrate (starch) in different inhibitor concentrations with error bars.



**Figure-S4:** Graph of compound **2**; Dixon plot of reciprocal of rate of reaction (velocities) vs different concentrations of inhibitor with error bars.

**Table-S1:** Kinetic studies data of selected compounds for *α*-amylase inhibition

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Comp. No.** | **Vmax (*µ*M/min/mg)** | **Km (mM)** | **Ki ((*µ*M)** | **Inhibition Type** |
| **2** | 1389.1 ± 3.2 | 1.7 ± 0.2 | 4.6 ± 0.2 | **Competitive type** |
| **3** | 1374.5 ± 4.0 | 17.9 ± 0.2 | 4.9 ± 0.1 | **Competitive type** |
| **4** | 1379.1 ± 3.7 | 18.5 ± 0.9 | 4.0 ± 0.2 | **Competitive type** |
| **7** | 1381.4 ± 4.2 | 8.6 ± 0.8 | 4.9 ± 0.1 | **Competitive type** |
| **9** | 1382.3 ± 4.3 | 7.1 ± 0.3 | 4.7 ± 0.1 | **Competitive type** |
| **11** | 1387.4 ± 1.9 | 11.7 ± 0.4 | 3.9 ± 0.2 | **Competitive type** |
| **Acarbose** | 1110.3 ± 1.8 | 9.9 ± 0.2 | 3.2 ± 0.4 | **Competitive type** |



**Figure-S5:** Interaction Profile of potent compounds against the *α*-amylase enzyme. **a-d** for compounds **2**, **4**, **7**, and **9**, respectively, double-sided arrow and dashes lines indicate pi-stacking and hydrogen interaction.

**Table-S2:** Interaction data for compounds **1-33**.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Comp.** | **Interaction details** | | | | | | **Docking score** |
| **Ligands** | **Receptor** | **Interaction** | **Distance** | **E cal/mol** | **Residue** |
| **1** | O 12  O 12 | NH1  NH2 | H-Acceptor H-Acceptor | 3-14  3.52 | -1.1  -0.6 | ARG319 (A)  ARG319 (A) | -4.29926062 |
| **2** | O 20  6-ring  O 11 | O  NH1  CA | H-donor  π-cation  π-cation | 3.00  3.66  3.50 | -1.7  -0.5  -0.9 | ASN430 (A)  ARG319 (A)  ARG267 (A) | -5.54966974 |
| **3** | C 19  O 21 | ODI  NH2 | H-donor  H-Acceptor | 3.24  2.76 | -0.6  -3.1 | ASP433 (A)  ARG319 (A) | -5.07143116 |
| **4** | O 11  6-ring | CE  NH1 | H-Acceptor π-cation | 3.05  3.51 | -1.0  -1.4 | LYS268 (A)  ARG319 (A) | -4.75101042 |
| **5** | 6-ring | NZ | π-cation | 3.71 | -1.3 | LYS268 (A) | -5.02969456 |
| **6** | O 22 | CE | H-Acceptor | 3.21 | -1.6 | LYS268 (A) | -5.0619216 |
| **7** | N 20  N 20 | O  NH2 | H-donor  H-Acceptor | 3.31  3.53 | -0.9  -0.7 | ASN430 (A)  ARG319 (A) | -5.00436354 |
| **8** | N 20  6-ring | NH1  NZ | H-Acceptor π-cation | 3.67  3.42 | -1.2  -1.8 | ARG319 (A)  LYS268 (A) | -5.19214249 |
| **9** | 6-ring  Cl 17 | NH2  CA | π-cation  H-Acceptor | 3.88  3.61 | -1.5  -0.7 | ARG319 (A)  ARG267 (A) | -4.95994854 |
| **10** | O 23 | N | H-Acceptor | 2.07 | -0.8 | ARG319 (A) | -5.19688082 |
| **11** | O 11  O 11 | CA  CE | H-Acceptor  H-Acceptor | 3.61  3.36 | -0.5  -0.9 | ARG267 (A)  LYS268 (A) | -5.196208 |
| **12** | O 20 | CA | H-Acceptor | 3.54 | -0.5 | ASP433 (A) | -5.08518839 |
| **13** | O 20  O 11 | ODI  CE | H-donor  H-Acceptor | 2.80  3.61 | -0.5  -0.9 | ASN431 (A)  LYS268 (A) | -5.50869513 |
| **14** | O 11  O 11 | CA  CE | H-Acceptor H-Acceptor | 3.27  3.55 | -0.7  -1.0 | ARG267 (A)  LYS268 (A) | -5.35262394 |
| **15** | O 11 | CA | H-Acceptor | 3.61 | -0.7 | ARG267 (A) | -4.99429464 |
| **16** | O 11 | CE | H-Acceptor | 3.58 | -1.0 | LYS268 (A) | -5.42532587 |
| **17** | O 11 | CA | H-Acceptor | 3.43 | -0.8 | ARG267 (A) | -5.30218649 |
| **18** | O 11 | CA | H-Acceptor | 3.42 | -0.7 | ARG267 (A) | -5.04802227 |
| **19** | O 11 | CE | H-Acceptor | 3.16 | -1.1 | LYS268 (A) | -5.06601286 |
| **20** | 5-ring | NZ | π-cation | 3.47 | -0.8 | LYS268 (A) | -5.12210989 |
| **21** | 5-ring | NZ | π-cation | 3.46 | -1.2 | LYS268 (A) | -4.99122 |
| **22** | O 11 | NZ | H-Acceptor | 3.25 | -2.7 | LYS268 (A) | -4.88413477 |
| **23** | O 11  5-ring | NZ  NZ | H-Acceptor π-cation | 3.39  3.47 | -1.9  -0.5 | LYS268 (A)  LYS268 (A) | -4.78715372 |
| **24** | S 18 | ODI | H-donor | 3.35 | -2.1 | ASP433 (A) | -4.8910594 |
| **25** | O 11  6-ring | CE  NH1 | H-Acceptor π-cation | 2.96  3.54 | -1.2  -0.5 | LYS268 (A)  ARG319 (A) | -4.77398682 |
| **26** | O 11 | CE | H-Acceptor | 3.17 | -1.1 | LYS268 (A) | -5.06489849 |
| **27** | NA | - | - | - | - | - | NA |
| **28** | NA | - | - | - | - | - | NA |
| **29** | NA | - | - | - | - | - | NA |
| **30** | NA | - | - | - | - | - | NA |
| **31** | NA | - | - | - | - | - | NA |
| **32** | NA | - | - | - | - | - | NA |
| **33** | 5-ring | CD | π-H | 3.58 | -0.5 | LYS268 (A) | -5.1667881 |

**Figure-S6:** Graphical representation of variation in DPPH and ABTS radical scavenging activity of compounds **1-33**